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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,546	01/18/2002	Gregory A. Demopulos	OMER118473	6615

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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	**PAPER NUMBER**
1618	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/031,546	DEMOPULOS ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38,39,44-54,60,73-76 and 81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *38,39,44-54,73-76,81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement of Papers Received: Amendment/Response dated 11/08/06.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38,39,44-54,59,60,73-76 and 81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific catabolic inhibiting agents such as MAP Kinase inhibitors and specific anabolic compounds such as interleukin, does not reasonably provide enablement for all possible compounds defined by their function of inhibiting catabolism or anabolic compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use or envision the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;
The claims are drawn to a method of inhibiting cartilage degradation comprising the administration of all compounds that can classify as anabolic chondroprotective agents and all compounds that can and do classify as catabolic inhibiting chondroprotective agents. Essentially every compound having an effect on cartilage tissue is claimed.
(B) The nature of the invention;
The nature of the invention is that of a method of preventing damage to cartilage using well compounds well know for these properties.
(C) The state of the prior art;
The prior art, acknowledges the cartilage repairing properties of the specific compounds recited in the dependent claims. Hunziker (USPN 5,206,023) establishes at the time of the invention chemotactic agents, defined separately by applicant, are useful in treating and

repairing defects or lesions in cartilage. These compounds include inhibitors of catabolic activity such as TNF-alpha and anabolic compounds such as TGF-betas (col. 7, lin. 62-col. 8, lin. 7).

(D) The level of one of ordinary skill;

One of ordinary skill would be able to combine compounds of known properties in order to combine and improve their result. However in order to meet the limits of the claims, an artisan would have to test and verify each and every compound to asses their anabolic and catabolic inhibiting properties.

(E) The level of predictability in the art;

Given the wide range of possible compounds, the level of predictability is low. Compounds would need to assayed and all properties determined before a combination can be made of the described compounds. This would cause undue experimentation for every known compound.

(F) The amount of direction provided by the inventor;

The inventor does not provide much direction since the specific compounds are known for treating cartilage damage. In vitro assays are presented in the specification yet no in vivo testing is provided. Further the combinations as claimed are not exemplified in the specification.

(G) The existence of working examples;

The specification does not appear to contain any working examples of composition combing the compounds as defined and being used in the manner recited in the claims. There do not appear to be any working examples of a cartilage repairing or treating composition created by the examples. The specification provides assays for determining the appropriate compounds that can be defined, as anabolic or catabolic inhibitors, yet is completely silent to in vivo testing. All examples occur within in vitro models of cartilage tissue. There are no working in vitro examples for the proposed combinations.

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

As discussed above, one of ordinary skill in the art would have to test every known compound to determine the anabolic properties and catabolic inhibiting properties of said compound. Extensive in vivo testing would be required on the part of the ordinary artisan.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 38,39,44-54,59,60,73-76 and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al (USPN 6,096,728 hereafter '728) and Hunziker (USPN 5,206,023 hereafter '023). The claims are drawn to method of inhibiting cartilage degradation in a joint comprising delivering to the joint a composition comprising two chondroprotective agents.

2. The '728 patent teaches a method and formulation for the treatment of inflammatory diseases (abstract). The method requires the administration of a formulation comprising Interleukin 1 inhibitors in combination with various therapeutic compounds and carriers (col. 25, lin. 52-65). The additional compounds include MAP kinase inhibitors such as SB203580 (col. 32, lin. 17), and anti-inflammatory agents when the composition is used for the treatment of chronic osteoarthritis, psoriatic arthritis and/or rheumatoid arthritis (col. 34, lin. 6-24). The compounds can be injected intra-articulately (col. 35, lin. 13-col. 36, lin. 60) before, during or after a trauma or surgical procedure (*Ibid.*). The reference is however silent to the inclusion of fibroblast growth factors.

3. The '023 patent teaches methods for the treatment and repair of defects of lesions in cartilage (abstract). The method includes the delivery via injection a composition comprising various therapeutic compounds such as fibroblast growth factors (col. 4, lin. 49-64) and chemo tactic agents such as tumor necrosis factors (col. 7, lin. 50-65). The growth factors are combined with other components in methods to treat defects in knee cartilage (examples).

4. Since both '728 and '023 disclose compositions for the treatment of cartilage damage, it would be well within the level of skill in the art to combine them in order to provide an improved

cartilage treatment composition. It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. *See* In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

5. With these things in mind it would have been obvious to combine the compounds of '023 and '728 in order to produce an improved method of treatment. The method of '728 requires a mixture of ingredients including anti-inflammatory agents, and inhibitors of catabolic action. It would be within the level of skill in the art to combine these compounds with those of '023 since the compounds of both references are useful in the treatment of damaged cartilage. It would have been obvious to make this combination with an expected result of an improved treatment method for damaged cartilage.

Response to Amendment

6. The Declaration filed under 37 CFR 1.132 filed 11/06/06 is insufficient to overcome the rejection of claims 38,39,44-54,59,60,73-76 and 81 based upon USC 103(a) as set forth in the last Office action because: the declaration provides specific examples of combinations related to the invention, yet which are not specifically represented in the claims. The examples of the declaration are not commensurate in scope with that of the instant claims. The declaration exemplifies a combination of IGF-1/IL-1Ra, IGF-1/SC514 or UO126, IGF-1/SC514 or SB239063, BMP family members/p38 inhibitor while the claims remain directed to all anabolic

chondroprotective agents combined with all inhibitors of catabolic activity. The declaration provides seven possible combinations while the claims recite hundred of possible combinations. The examples in fact provide supports for the prior art ('728 patent) of combining cartilage-protecting agents in order to provide an improved result over the individual compounds. For these reasons the claims remain obviated by the combination of the prior art.

Response to Arguments

7. Applicant's arguments filed 11/08/06 have been fully considered but they are not persuasive. Applicant argues that:

a. There would be no undue experimentation regarding the making or using of the claimed invention.

b. There is no motivation to combine an anabolic compound with a compound for inhibiting catabolic activity as in the claimed invention.

8. Regarding argument a., it remains the position of the Examiner that since the specification provides no in vivo examples of the proposed, claimed combination an artisan or ordinary skill would be subject to undue experimentation to arrive at and make/use the claimed invention. The examples are in vitro models that inhibit particular compound suspected in cartilage damage. However these models are never transferred to an in vivo model and tested. For these reasons the claims are commensurate in scope tithe specification. The specification has not shown that the combination of compounds (anabolic mixed with a catabolic inhibitor) can inhibit cartilage damage for each and every instance of cartilage damage in a human joint. For these reasons at least the claims present a level of undue experimentation.

9. Regarding argument b., it is the position of the Examiner that the motivation to combine chondroprotective agents in order to increase their overall effectiveness. The Collins reference combines similar anabolic compounds while increasing their overall effect. In the reference the interleukin receptor agonists are combined with other agents such as hyaluronic acid, COX-2 inhibitors and the like (col. 32, lin. 10-34). These combinations provide an improved treatment for inflammatory disorders in joints (figures). Collins provides motivation to combine similar compounds with similar purposes in order to improve the overall result. Hunziker provides further motivation. The reference discloses compounds useful in the treatment and repair of lesions and defects in cartilage. The compounds recited include tumor necrosis factors (TNF alphas) described by applicant as inhibitors of cartilage catabolism and TGF-betas, described by applicant as anabolic agents. This disclosure provides sufficient motivation to combine both anabolic and catabolic inhibiting compounds in order to repair and treat cartilage damage. The claims are drawn to the inhibition of cartilage damage, which the prior art discloses. The Hunziker reference, though not teaching all of the specific compounds, does in fact discloses that anabolic and catabolic inhibiting compounds can be used to treat cartilage damage. Collins provides the specific MAP kinase inhibitor, and other compounds such as anti-inflammatory agents. The Hunziker provide the motivation to combine compounds that help treat cartilage damage, even though they might be classified differently. For these reasons the claims remain obviated by the prior art.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 571-272-0608. The examiner can normally be reached on M-F 7:00-4:30 every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Micah-Paul Young
Examiner
Art Unit 1618

MP Young

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER